UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

Date: 12-JULY-2006

Subject: Myclobutanil. **REVISED** Human Health Risk Assessment for Proposed Uses on Hops and Home Garden Fruit Trees, Nut Trees, Berries, Mint and Vegetables. PC Code: 128857. PP#: 1E6265. DP#: D330235. Decision #: 357983.

From: Jennifer R. Tyler, Chemist
P.V. Shah, Ph.D.
Mark I. Dow, Ph. D., Biologist
Registration Action Branch 1
Health Effects Division (7509C)

Timothy C. Dole, CIH, Industrial Hygienist
Reregistration Branch 1 (RRB1)/HED (7509C)

Thru: P.V. Shah, Ph.D., Branch Senior Scientist
RAB1/HED (7509C)

Felecia Fort, Acting Branch Chief
RAB1/HED (7509C)

To: Mary Waller, PM Team 21
Fungicide Branch
Registration Division (RD; 7505C)

Note: The following memorandum supersedes the HED Human health risk assessment dated 6/14/06 (J. Tyler; DP# 318501). Dow AgroSciences agreed to revise its current labels to include a maximum application rate of 0.62-0.65 lb ai/A for residential use on turf (personal communication between R. Brinkmeyer and J. Tyler, 7/10/06). The company will submit revised labels to include these changes.

INTRODUCTION

Interregional Research Project No. 4 (IR-4), on behalf of the Washington State Hops Commission that represents all United States (U.S.) hops growers, has submitted a request for the use of the triazole fungicide myclobutanil [α-butyl-α-(4-chlorophenyl)-1*H*-1,2,4-triazole-1-propanenitrile] on hops. IR-4 has proposed a tolerance, expressed as the parent compound and

its alcohol metabolite α- (3-hydroxybutyl)-α- (4-chlorophenyl)-1*H*-1, 2,4-triazole-1-propanenitrile (free and bound) (RH-9090), of 10.0 ppm on dried hops. Concurrently, the petitioner has submitted a request for Section 3 registration of the products Rally® 40W Agricultural Fungicide (EPA Reg No. 707-215) and Nova® 40W Agricultural Fungicide (EPA Reg No. 707-221), both of which are packaged as water-soluble pouches containing 40% myclobutanil as the active ingredient (ai), on hops.

In addition, Chemsico has requested a label amendment to add home garden uses on almonds, apples, mayhaw, berries, grapes, peppermint, spearmint, stone fruits, strawberries, asparagus, cucurbits, snap beans and tomatoes to the Chemsico Fungicide M label (EPA Reg. No. 9688-123), a product containing 1.55% myclobutanil as the ai.

NOTE: HED previously completed a Section 3 human-health risk assessment for the use of myclobutanil on several commodities (Memo, J. Rowell, *et al.* 3/14/00; D244901), and RD recently completed a Section 18 Emergency Exemption assessment for the use of myclobutanil on soybeans and legume vegetables (Memo, W. Cutchin, 8/9/05; D317318). This document contains only those aspects of the risk assessment that are affected by the addition of the proposed new uses of myclobutanil. The following information from the previous risk assessments on myclobutanil can be applied directly to this action:

- Physical/Chemical Properties (page 11 of 3/14/00 memo).

The following should also be noted that, since the completion of the 3/14/00 risk assessment,

- RAB1 toxicologists re-evaluated the myclobutanil toxicology database and concluded that the 28-day dermal toxicity study previously used for short-term dermal risk assessment is not appropriate. A two-generation reproduction study in rats was selected because the effects of concern (atrophy of the testes and prostate) seen at a lowest observed adverse effect level (LOAEL) of 50 mg/kg/day may not be protective if the endpoints were based on the 28-day dermal toxicity study. In addition, there were no effects of concern identified in the 28-day dermal toxicity study [no observed adverse effect level (NOAEL) of 100 mg/kg/day was the highest dose tested].
- EPA conducted a human-health assessment for aggregate exposure to 1,2,4-triazole and triazolylalanine/triazolylacetic acid in a separate document in order to support the extension of existing and granting of new parent triazole-derivative fungicide tolerances (Memo Doherty, et al., 12/22/05; DP# 322215).

In this memo, dietary, residential, occupational and aggregate risks were re-evaluated based on the addition of aforementioned uses to the myclobutanil use pattern.

Conclusions/Recommendations: Aggregate risk assessments were performed for acute (food and drinking water), short-term (food, drinking water and residential), intermediate-term (food, drinking water and residential), and chronic aggregate exposure (food and drinking water). The acute and chronic aggregate risks associated with the proposed uses of myclobutanil do not exceed HED's level of concern for the general U.S. population or any population subgroup. For the general U.S. population, the short-term handler and short- and intermediate-term post-application aggregate margins of exposure (MOEs) are greater than 100; and, therefore, do not exceed HED's level of concern (MOE <100). For children/toddlers, the short- and intermediate-term aggregate MOE is 63 for the "playing on lawn" scenario using the turf application rate of 1.36 lb ai/A, but is 130 for the same scenario using the 0.62 lb ai/A turf application rate. It should be noted that the high rate of 1.36 lb ai/A is from the Eagle® 20EW label (EPA Reg. No. 62719-463), which appears to be primarily intended for turf use on golf courses because it has the statement "A systemic, protective and curative fungicide for disease control in turf grass (including golf course fairways, roughs, tee boxes and greens)." However, as there is no specific language prohibiting use on residential turf, it was assumed that this product could be used on residential turf.

The ***residue chemistry and toxicological databases*** are adequate to support the following:

- The requested label amendment to add home garden uses on almonds, apples, mayhaw, berries, grapes, peppermint, spearmint, stone fruits, strawberries, asparagus, cucurbits, snap beans and tomatoes to the Chemsico Fungicide M label (EPA Reg. No.9688-123).
- The establishment of unconditional registration and a permanent tolerance of 10 ppm for the combined residues of myclobutanil and its alcohol metabolite α- (3-hydroxybutyl)-α-(4-chlorophenyl)-1H-1, 2,4-triazole-1-propanenitrile (free and bound) in/on hop, dried cones.

However, as the short- and intermediate-term aggregate risk for children/toddlers are of concern (MOE<100), the ***occupational and residential exposure database*** is not adequate to support the proposed uses at this time. The short- and intermediate-term aggregate risk would be acceptable if the myclobutanil product labels with turf uses are amended to specify at maximum application rate of 0.62 lb ai/A on residential turf.

1.0 Background

Myclobutanil is a contact triazole fungicide, which is applied to prevent fungal outbreaks. In agricultural and commercial settings it has a variety of uses including fruits, vegetables, ornamentals and turf. In the residential setting, the existing uses include turf and ornamentals. The proposed new uses include hops as well as home garden uses on fruit trees, nut trees, berries, mint and vegetables.

2.0 Hazard Characterization/Toxicity Endpoint Selection

2.1 Hazard Characterization: The toxicological database for myclobutanil is adequate to support registration and tolerances. There are no data gaps. Myclobutanil has low acute toxicity with the exception for ocular irritation. It is toxicity category III for oral acute toxicity, category IV for dermal and inhalation acute toxicity and dermal irritation. Myclobutanil is category I for ocular irritation and the technical is a dermal sensitizer. However, formulation containing 40% myclobutanil was not sensitizing. In rat subchronic and chronic toxicity studies, the primary target organs are liver and testes. Liver effects, following subchronic exposure, include hypertrophy, hepatocellular necrosis and increased liver weight. There is decreased testicular weight and testicular atrophy. Chronic exposure to the rat also results in hepatocellular vacuolization and additional testicular effects, which include bilateral aspermatogenesis, increased incidences of hypospermia and cellular debris in the epididymides and increased incidences of arteritis/periarteritis in the testes. With the exception of testicular effects, subchronic and chronic exposures in the mouse result in a toxicity profile similar to the rat. The mouse, following chronic exposure, has, in addition, increased Kupffer cell pigmentation, periportal punctate vacuolation, and individual cell necrosis of the liver. There is no evidence of carcinogenic potential in either the rat or mouse. In the subchronic dog, there are hepatocellular hypertrophy, increased relative and absolute liver weight and increased alkaline phosphatase. In the chronic dog study, liver toxicity is similar with the addition of "ballooned" hepatocytes and increases in SGPT and GGT. Signs of toxicity observed in the rat 28-day dermal studies (studies on the 40WP and 2EC formulations) are limited to dermal irritation. There is no evidence of systemic toxicity in either study. There is no evidence of increased susceptibility in either of the developmental toxicity studies or the reproduction study. In the rat developmental toxicity study, maternal toxicity, which included rough hair coat and salivation, occurs at the same dose level as increases in incidences of 14^{th} rudimentary and 7^{th} cervical ribs in the fetuses. At the next higher dose there is also alopecia, desquamation and red exudate around the mouth in the dams. In the rabbit developmental toxicity study there is reduced body weight and body weight gain during the dosing period, clinical signs of toxicity and a possible increase in abortions in the does at the same dose level that there are increased resorptions, decreased litter size and decreased viability index. The maternal toxicity in the rat reproduction study includes increased liver weights and hepatocellular hypertrophy. Reproductive effects occur at the same dose and include increased incidences in the number of still born pups and atrophy of the testes, epididymides and prostate. Developmental effects occurring at the same dose in the reproduction study include decreased pup body weight gain during lactation. Myclobutanil is rapidly absorbed and excreted with complete elimination by 96 hours. There is extensive metabolism prior to excretion with elimination of radiolabeled material evenly distributed between urine and feces. There is no evidence of tissue accumulation. There is no concern for mutagenic activity. Myclobutanil was determined to be not carcinogenic in two acceptable animal studies. Therefore, it was classified as a "Group E" chemical (evidence of noncarcinogenicity for humans).

2.2 Toxicity Endpoint Selection: The doses and toxicological endpoints selected for various exposure scenarios are summarized in Table 2.1. RAB1 toxicologists recently re-evaluated the myclobutanil toxicology database and concluded that the 28-day dermal toxicity study previously used for short-term dermal risk assessment is not appropriate. A two-generation reproduction study in rats was selected because the effects of concern (atrophy of the testes and prostate) seen at a LOAEL of 50 mg/kg/day may not be protective if the endpoints were based on the 28-day dermal toxicity study. In addition, there were no effects of concern identified in the 28-day dermal toxicity study (NOAEL of 100 mg/kg/day was the highest dose tested).

Table 2.1. Summary of Toxicological Dose and Endpoints for Myclobutanil for Use in Human Risk Assessment

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects
Acute Dietary females 13-50 years of age	NOAEL = 60 mg/kg/day UF = 100 **Acute RfD** = 0.60 mg/kg/day	FQPA SF = 1x **aPAD** = acute RfD / FQPA SF = 0.60 mg/kg/day	Developmental Toxicity - rabbit[1] LOAEL = 200 mg/kg/day based on increased resorptions, decreased litter size and a decrease in the viability index.
Acute Dietary general population including infants and children	none	not applicable	not applicable
Chronic Dietary all populations	NOAEL= 2.49 mg/kg/day UF = 100 **Chronic RfD** = 0.025 mg/kg/day	FQPA SF = 1x **cPAD** = chronic RfD / FQPA SF = 0.025 mg/kg/day	Chronic Toxicity/ Carcinogenicity - rat LOAEL = 9.94 mg/kg/day based on decreased testicular weights and increased testicular atrophy.
Short-Term Dermal (1-30 days) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (dermal absorption rate = 50%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Intermediate-Term Dermal (1-6 months) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (dermal absorption rate = 50%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Long-Term Dermal (> 6 months) (Occupational/ Residential)	oral study NOAEL= 2.49 mg/kg/day (dermal absorption rate = 50%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	Chronic Toxicity/ Carcinogenicity – rat LOAEL = 9.94 mg/kg/day based on decreased testicular weights and increased testicular atrophy.

Table 2.1. Summary of Toxicological Dose and Endpoints for Myclobutanil for Use in Human Risk Assessment

Exposure Scenario	Dose Used in Risk Assessment, UF	FQPA SF and Endpoint for Risk Assessment	Study and Toxicological Effects
Short-Term Inhalation (1-30 days) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Intermediate-Term Inhalation (1 –6 months) (Occupational/ Residential)	oral study NOAEL= 10 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	2 Generation Reproduction Toxicity - rat LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.
Long-Term Inhalation (>6 months) (Occupational/ Residential)	oral study NOAEL= 2.49 mg/kg/day (inhalation absorption rate = 100%)	**acceptable MOE** = 100 (Occupational) **acceptable MOE** = 100 (Residential, includes the FQPA SF)	Chronic Toxicity/ Carcinogenicity - rat LOAEL = 9.94 mg/kg/day based on decreased testicular weights and increased testicular atrophy.
Cancer (oral, dermal, inhalation)	"Group E"	not applicable	not applicable

1. The HIARC document (dated 9/2/99) table incorrectly lists this as rat.

3.0 Food Quality Protection Act (FQPA) Assessment

The FQPA Safety Factor Committee (SFC) met on August 16, 1999 (HED Doc. No. 013734, dated 9/13/99) to evaluate the hazard and exposure data for myclobutanil. The committee recommended that the FQPA Safety Factor (SF) (as required by FQPA of August 3, 1996) be reduced to 1x in assessing the risk posed by this chemical. The myclobutanil risk assessment team re-evaluated the quality of the toxicology and exposure data; and, based on these data, recommended that the FQPA SF be reduced to 1x (Memo, J. Tyler. The recommendation is based on the following:

- There are no toxicity data gaps in the consideration of the FQPA SF.
- The Hazard Identification Assessment Review Committee (HIARC) concluded that there was no evidence of increased susceptibility in the developmental toxicity studies with rats and rabbits.
- HIARC determined that a developmental neurotoxicity study is not required because neurotoxic compounds of similar structure were not identified and there was no evidence of neurotoxicity in the current toxicity database.
- The exposure assessments will not underestimate the potential dietary (food and drinking water) and residential (non-occupational) exposures for infants and children from the use of myclobutanil.
- The acute dietary food exposure assessment (females 13-49 years old only) utilizes existing and proposed tolerance level residues and 100% crop treated (CT) information for all commodities. By using these screening-level assessments, actual exposures/risks will not be underestimated.

- The chronic dietary food exposure assessment utilizes existing and proposed tolerance level residues; USDA Pesticide Data Program (PDP) monitoring data for apple juice, bananas (not plantains) and milk; average % CT data verified by the Biological Economic and Analysis Division (BEAD) for apple (except juice), apricots, artichokes, asparagus, sugar beet, blackberry, and tomatoes; and 100% CT information for all other registered and proposed uses. The chronic assessment is somewhat refined and based on reliable data and will not underestimate exposure/risk.
- The dietary drinking water assessment utilizes water concentration values generated by model and associated modeling parameters, which are designed to provide conservative, health protective, high-end estimates of water concentrations which will not likely be exceeded.
- The residential handler assessment is based upon the residential standard operating procedures (SOPs) and utilized unit exposure data from the Outdoor Residential Exposure Task Force (ORETF) and the Pesticide Handlers Exposure Database (PHED). The residential post-application assessment is based upon chemical-specific turf transferable residue (TTR) data and DFR data. The chemical-specific study data as well as the surrogate study data used are reliable and also are not expected to underestimate risk to adults as well as to children. In a few cases where chemical-specific data were not available, the SOPs were used alone. The residential SOPs are based upon reasonable "worst-case" assumptions and are not expected to underestimate risk. These assessments of exposure are not likely to underestimate the resulting estimates of risk from exposure to myclobutanil.

4.0 Endocrine Disruption

EPA is required under the Federal Food Drug and Cosmetic Act (FFDCA), as amended by FQPA, to develop a screening program to determine whether certain substances (including all pesticide active and other ingredients) "may have an effect in humans that is similar to an effect produced by a naturally occurring estrogen, or other such endocrine effects as the Administrator may designate." Following the recommendations of its Endocrine Disruptor Screening and Testing Advisory Committee (EDSTAC), EPA determined that there were scientific bases for including, as part of the program, the androgen and thyroid hormone systems, in addition to the estrogen hormone system. EPA also adopted EDSTAC's recommendation that the Program include evaluations of potential effects in wildlife. For pesticide chemicals, EPA will use FIFRA and, to the extent that effects in wildlife may help determine whether a substance may have an effect in humans, FFDCA has authority to require the wildlife evaluations. As the science develops and resources allow, screening of additional hormone systems may be added to the Endocrine Disruptor Screening Program (EDSP).

When the appropriate screening and/or testing protocols being considered under the Agency's EDSP have been developed, myclobutanil may be subjected to additional screening and/or testing to better characterize effects related to endocrine disruption.

5.0 Registered/Proposed Application Scenarios

5.1 Registered Uses: Myclobutanil is a contact fungicide that is applied to prevent fungal outbreaks. In agricultural and commercial settings, it has a variety of uses including fruits, vegetables, ornamentals, and turf. In the residential setting, the existing uses include turf and ornamentals. Permanent tolerances are currently established for the combined residues of myclobutanil and its RH-9090 metabolite (free and bound) in/on a variety of raw agricultural commodities (RACs) at levels ranging from 0.02 to 25.0 ppm and in meat, milk, poultry, and

eggs at levels ranging from 0.02 to 1.0 ppm [40 CFR §180.443(a)]. In addition, tolerances in conjunction with Section 18 registrations have been established for a number of RACs under 40 CFR §180.443(b). Tolerances for indirect or inadvertent residues of myclobutanil have been established for several crop groups under 40 CFR §180.443(d).

5.2 Proposed Uses: For the proposed agricultural use on hops, specimen labels were provided for use of myclobutanil formulated as Rally® 40W Agricultural Fungicide (EPA Reg No. 707-215) and Nova® 40W Agricultural Fungicide (EPA Reg No. 707-221), both of which are packaged as water-soluble pouches containing 40% ai. For the proposed home garden uses, a specimen label was provided for use of myclobutanil formulated as Fungicide M (EPA Reg. No. 9688-123), which contains 1.55% ai. Summaries of the proposed use patterns are provided in Attachment 1.

HED Conclusions: Labels have been provided for use of myclobutanil formulated as Rally® 40W, Nova® 40W, and Fungicide M. No deficiencies in the labels were noted. There are currently permanent tolerances under 40 CFR §180.443 for the crops listed in Attachment 1. Although the proposed home garden use directions differ slightly from the registered agricultural uses for some commodities, the current tolerances are adequate to support the proposed home garden uses.

6.0 Residue Chemistry Considerations

Residue chemistry memo - DP# 275142, J. Tyler, 6/4/01

6.1 Nature of the Residue - Plants: No plant metabolism data were submitted with this petition. Plant metabolism studies on wheat, grapes, and apples have previously been submitted and reviewed (PP#4G3149 and PP#7G3479), and were summarized in HED review of PP#2F4155 (DP Barcode D183273, D. Davis, 2/8/93). The requirement to conduct a tomato metabolism study, in conjunction with PP#1F4030, was waived (DP Barcode D203587, J. Stokes, 7/13/94). By translation of metabolism data from wheat, grapes and apples, the qualitative nature of the residue in hops is adequately understood. The residues of concern are the parent myclobutanil and its RH-9090 metabolite (free and bound). Additionally, the Agency does have concern about potential toxicity to 1,2,4-triazole and two conjugates, triazole alanine and triazole acetic acid, metabolites common to most of the triazole fungicides. To support the extension of existing and granting of new parent triazole-derivative fungicide tolerances, EPA conducted a human-health assessment for aggregate exposure to 1,2,4-triazole and triazolylalanine/triazolylacetic acid in a separate document (Memo Doherty, *et al.*, 12/22/05; DP# 322215).

6.2 Residue Analytical and Multiresidue Methods: An adequate enforcement method [Rohm and Haas Gas-Liquid Chromatography (GLC) Method 34S-88-10] is available for enforcement of the proposed tolerances. Quantitation is by GLC using a nitrogen/phosphorus (N/P) detector for parent myclobutanil and an electron-capture detector (Ni_{63}) for residues measured as RH-9090. EPA has conducted a successful method validation of Method 34S-88-

10, and the method has been forwarded to the Food and Drug Administration (FDA) for inclusion in Pesticide Analytical Methods (PAM), Volume II (PP#7F3476 and FAP#7H5524, M. J. Nelson, 4/14/88 and 7/18/89). Samples of hops from the submitted field trials were analyzed for residues of myclobutanil and the metabolite RH-9090 using Method TR-310-84-13. Concurrent method recovery data were acceptable.

Multiresidue method data are available in the 2/97 FDA PESTDATA database PAM, Volume I, Appendix I. Residues of myclobutanil are adequately recovered (>80%) using Multiresidue Method Section 302 (Luke Method; Protocol D), but are not recovered using Multiresidue Method Sections 303 (Mills, Onley, Gaither Method; Protocol E, non-fatty foods) or 304 (Mills Method; Protocol E, fatty foods). Residues of the metabolite RH-9090 were poorly recovered (30-55%) using Multiresidue Method Section 302 (Luke Method; Protocol D); the metabolite is not recovered using Multiresidue Method Sections 303 (Mills, Onley, Gaither Method; Protocol E, non-fatty foods) and 304 (Mills Method; Protocol E, fatty foods).

6.3 Storage Stability Data: The concurrent storage stability data, provided by the Interregional Research Project No. 4 (IR-4), are marginally adequate because the storage stability at zero time was not measured/provided; this information is vital in determining the percent decline of residues over time. Although marginal, the concurrent storage stability data from the current submissions indicate that fortified residues of myclobutanil and its RH-9090 metabolite are relatively stable during frozen storage for up to 82 days (~ 4 months) in/on hops. The maximum interval that the hops samples from the residue field trials remained in frozen storage prior to analysis was 70 days. HED concludes that myclobutanil and its metabolite are stable for this time period. HED notes that additional storage stability data from previous myclobutanil petitions indicate that residues of myclobutanil and its RH-9090 metabolite are stable under frozen storage conditions for up to 3 years in/on apples (PP# 7F3476, M.J. Nelson, 2/8/88) and grapes (PP#7F3476, M.J. Nelson, 4/26/88).

6.4 Crop Field Trials and Processed Food and Feed: The submitted residue data on hops are adequate and indicate that the combined residues of myclobutanil and its metabolite RH-9090 will not exceed the proposed tolerance level of 10 ppm in/on hops, dried when harvested 14 days following the last of nine foliar applications, with 7- to 12-day RTIs, of the 40% WP formulation at 0.125-0.25 lb. ai/A/application (1x the maximum proposed seasonal application rate). Therefore, the available residue data support a tolerance of 10 ppm for residues of myclobutanil and its alcohol metabolite in/on "hop, dried cones." No processed food/feed items are associated with hops. Therefore, data pertaining to the magnitude of myclobutanil residues in processed commodities are not required.

6.5 International Considerations: There are no current Canadian or Mexican maximum residue limits (MRLs) for residues of myclobutanil in/on hops. However, there is a Codex MRL of 2 ppm for the parent compound myclobutanil in/on hops, dry. HED has concluded the submitted residue chemistry data support a tolerance of 10 ppm for residues of myclobutanil and its alcohol metabolite RH-9090 (free and bound). Therefore, harmonization with the Codex MRL is not possible.

7.0 Drinking Water Considerations

Drinking water assessment memo - DP# 290167 and D289700, T. Nguyen, 6/9/03

The Environmental Fate and Effects Division (EFED) provided Estimated Drinking Water Concentrations (EDWCs) of myclobutanil in ground and surface water using Food Quality Protection Act (FQPA) Index Reservoir Screening Tool (FIRST) and Screening Concentration in Ground Water (SCI-GROW), respectively. The assessment was based on hops, which has the highest use rate among all existing uses (15 applications per year and 0.65 lb ai/A per application at 14-day intervals). EFED calculated the acute (peak) and chronic (56-day) EDWCs for myclobutanil in surface water to be 333 ppb and 86 ppb, respectively. The ground water EDWC for both acute and chronic exposures in estimated as 3.2 ppb.

8.0 Dietary Risks (Food and Drinking Water)

Dietary exposure and risk assessment - DP# 319228, J. Tyler, 6/8/06

Acute (females 13-49 years old) and chronic dietary exposure (general U.S. population and all population subgroups) assessments were conducted using the Dietary Exposure Evaluation Model - Food Commodity Intake Database™ (DEEM-FCID™; ver. 2.03) program which incorporates consumption data from the United Stated Department of Agriculture's (USDA's) Continuing Surveys of Food Intakes by Individuals (CSFII), 1994-1996 and 1998. The 1994-96, 98 data are based on the reported consumption of more than 20,000 individuals over two non-consecutive survey days. Foods "as consumed" (e.g., apple pie) are linked to EPA-defined food commodities (e.g. apples, peeled fruit - cooked; fresh or N/S; baked; or wheat flour - cooked; fresh or N/S, baked) using publicly available recipe translation files developed jointly by USDA/ARS and EPA. Consumption data are averaged for the entire U.S. population and within population subgroups for chronic exposure assessment, but are retained as individual consumption events for acute exposure assessment.

For chronic exposure and risk assessment, an estimate of the residue level in each food or food-form (e.g., orange or orange juice) on the food commodity residue list is multiplied by the average daily consumption estimate for that food/food form. The resulting residue consumption estimate for each food/food form is summed with the residue consumption estimates for all other food/food forms on the commodity residue list to arrive at the total average estimated exposure. Exposure is expressed in mg/kg body weight/day and as a percent of the chronic population adjusted dose (cPAD). This procedure is performed for each population subgroup.

For acute exposure assessments, individual one-day food consumption data are used on an individual-by-individual basis. The reported consumption amounts of each food item can be multiplied by a residue point estimate and summed to obtain a total daily pesticide exposure for a deterministic (Tier 1 or Tier 2) exposure assessment, or "matched" in multiple random pairings with residue values and then summed in a probabilistic (Tier 3/4) assessment. The resulting distribution of exposures is expressed as a percentage of the acute population adjusted dose

(aPAD) on both a user (*i.e.*, those who reported eating relevant commodities/food forms) and a per-capita (*i.e.*, those who reported eating the relevant commodities as well as those who did not) basis. In accordance with HED policy, per capita exposure and risk are reported for all tiers of analysis. However, for Tiers 1 and 2, significant differences in user vs. per capita exposure and risk are identified and noted in the risk assessment.

HED's level of concern is when the exposure is greater than 100% of the PAD. That is, estimated exposures above this level are of concern, while estimated exposures at or below this level are not of concern. The DEEM-FCID™ analysis estimates the dietary exposure of the U.S. population and 26 population subgroups. The results reported in Table 8.1 are for the U.S. Population, all infants (<1 year old), children 1-2 years old, children 3-5 years old, children 6-12 years old, youth 13-19 years old, females 13-49 years old, males 20-49 years old, and adults 50+ years old.

8.1 Acute Dietary Exposure Estimates: An acute dietary exposure assessment was performed for females 13-49 years old (no endpoint was identified for the general U.S. population or any other population subgroup) using tolerance-level residues and 100% CT information for all registered and proposed uses. Drinking water was incorporated directly in the dietary assessment using the acute (peak) concentration for surface water generated by the FIRST model. These assessments conclude that the acute dietary exposure estimates (95th percentile) are below HED's level of concern (<100% of the aPAD) for females 13-49 years old at 4.2% of the aPAD.

8.2 Chronic Dietary Exposure Estimates: A refined, chronic dietary exposure assessment was performed for the general U.S. population and various population subgroups using USDA Pesticide Data Program (PDP) monitoring data for apple juice, bananas (not plantains) and milk, registered and proposed tolerance for all other commodities; average % CT information for apple (except juice), apricots, artichokes, asparagus, sugar beet, blackberry, and tomatoes; and 100% CT information for all other registered and proposed uses. Drinking water was incorporated directly into the dietary assessment using the chronic (annual average) concentration for surface water generated by the FIRST model. This assessment concludes that the chronic dietary exposure estimates are below HED's level of concern (<100% of the cPAD) for the general U.S. population (15% of the cPAD) and all population subgroups. The most highly exposed population subgroup is all infants (<1 year old) at 36% of the cPAD.

Table 8.1. Summary of Dietary Exposure and Risk for Myclobutanil.

Population Subgroup	Acute Dietary[1]		Chronic Dietary[2]	
	Dietary Exposure (mg/kg/day)	% aPAD	Dietary Exposure (mg/kg/day)	% cPAD
U.S. Population (total)	NA		0.003842	15
All Infants (< 1 year old)			**0.009005**	**36**
Children 1-2 years old			0.007697	31
Children 3-5 years old			0.006435	26
Children 6-12 years old			0.004189	17
Youth 13-19 years old			0.002840	11
Adults 20-49 years old			0.003418	14
Adults 50+ years old			0.003595	14
Females 13-49 years old	**0.025154**	**4.2**	0.003320	13

[1] Acute dietary endpoint of 0.6 mg/kg/day for females 13-49 years old. No acute dietary endpoint was chosen for the general U.S. population, including infants and children.
[2] Chronic dietary endpoint of 0.025 mg/kg/day applies to the general U.S. population and all population subgroups.

9.0 Residential Exposure

Residential exposure and risk assessment memo - DP# 319227, T. Dole

Myclobutanil, formulated as Chemsico Fungicide M, is being proposed for use on home gardens (see Attachment 1). In addition, end-use products containing the active ingredient, myclobutanil, are marketed for homeowner use on turf, roses, flowers, shrubs and trees. The homeowner use with the greatest potential for exposure is small-scale lawn application. Since myclobutanil is applied at 7- to 14-day intervals, only short-term exposure is expected for the residential handler. Short- and intermediate-term residential post-application exposures are also expected.

The NOAEL of 10 mg/kg/day was used for assessing short- and intermediate-term dermal, inhalation and incidental oral exposures. This NOAEL is from a 2-generation reproduction toxicity study in rats which testicular atrophy (in P_2 generation), an increase in the number of still born pups and decreased body weight gain during lactation (in both generations) were observed with a LOAEL of 50 mg/kg/day. A dermal absorption factor of 50% was used because the dermal endpoint was based upon an oral study. Chronic exposures are not expected due to the seasonal and intermittent nature of the existing and proposed uses.

A residential non-dietary exposure and risk assessment was conducted in support of the proposed home garden uses of myclobutanil. The assessment addresses residential risk from these proposed uses and also includes updated assessments for the existing residential uses of other

products on turf and ornamentals. In addition, the assessment has been updated to incorporate exposure factor changes that have taken place since the last myclobutanil residential exposure assessment was completed (Memo, D. Vogel, 3/7/00; D264191).

9.1 Residential Handler Exposures and Risks: The anticipated use patterns and current labeling indicate that a variety of application equipment could be used by the homeowner to apply myclobutanil to ornamental plants, shrubs, fruit trees, home garden vegetables and lawns. Therefore, the following scenarios were assessed.

1 Aerosol Spray Can Application to Ornamentals and Fruit Trees
2 Hose End Sprayer Application to Ornamentals and Fruit Trees
3 Low-pressure (LP) Handwand Application to Ornamentals
4 LP Handwand Application to Vegetables
5 Ready to use (RTU) Sprayer Application to Vegetables
6 Hose End Sprayer Application to Vegetables
7 Hose End Sprayer - Mix Your Own - Application to Turf
8 Hose End Sprayer - Ready to Use - Application to Turf
9 Belly Grinder Application to Turf
10 Broadcast Spreader Application to Turf

Unit exposure data were either taken from PHED or the home garden and turf application studies that were sponsored by the Outdoor Residential Exposure Task Force (ORETF). The assumptions and factors used in the risk calculations include:

- Both the proposed uses on the Chemsico Fungicide M Label and existing uses on other myclobutanil labels were assessed. The other labels include granular and aerosol can products that are used on turf and ornamentals.
- The application rates for the new uses were taken from the proposed Chemsico fungicide label and are roughly the same as the rates on agricultural and commercial labels if the spray volume is 87 gallons per acre (GPA) for turf, 100 GPA for most crops and 400 GPA for fruit trees. A listing of these rates is included in Attachment 1.
- The application rates for the existing uses were taken from the existing labels.
- The area treated per day (1000 square feet) was taken from Scientific Advisory Council (ExpoSAC) Policy #12 "Recommended Revisions to the Standard Operating Procedures for Residential Exposure Assessments" of 2/22/01. This value is based upon the results of the National Home Garden Survey and is applicable for the four application methods considered.

The dermal and inhalation MOEs were combined because the dermal and inhalation endpoints were selected from the same oral study and are summarized in Table 9.1. The MOEs for residential handlers range from 180 to 55,000 with the highest risks (*i.e.* the lowest MOEs) associated with the mixing, loading and applying myclobutanil to turf with a mix your own hose end sprayer at the highest rate of 1.36 lb ai/A. With the lower application rate of 0.62 lbs ai/A, the lowest MOE is 370.

Table 9.1. Myclobutanil Residential Handler Risks.

Exposure Scenario (all are mix/load/apply)	Use Site	Application Rate (lb ai/A)	Amount Used or Area Treated	Absorbed Daily Dose (mg/kg/day)	Combined MOE
Aerosol Spray Can	Ornamentals	0.012% ai per 15 ounce can	1 can per day	0.00018	55000
Hose End Sprayer	Ornamentals Fruit Trees Nut Trees Grapes	0.25	0.023 acre/day (1000 square feet)	0.0016	6200
LP Handwand				0.0023	4300
LP Handwand	Vegetables Berries Mint	0.125	0.023 acre/day (1000 square feet)	0.00078	13000
RTU Sprayer				0.0011	9000
Hose End Sprayer				0.00070	14000
Hose End Sprayer - Mix Your Own	Turf	1.36	0.5 acre/day	0.054	180
Hose End Sprayer - Ready to Use				0.0130	790
Hose End Sprayer - Mix Your Own	Turf	0.62	0.5 acre/day	0.0250	370
Hose End Sprayer - Ready to Use				0.0059	1600
Belly Grinder	Turf	1.36	0.023	0.0250	410
Broadcast Spreader			0.5	0.0033	3000

9.2 Home Garden Post-application Exposures and Risks: Home garden post-application exposures can occur when home gardeners perform tasks such as weeding, pruning or hand harvesting following application of myclobutanil. In order to address these risks, the post-application exposure to home gardens and orchard scenarios were assessed based upon the Residential SOP 3.0 for Garden Plants and SOP 4.0 for Trees.

Two DFR studies on grapes in California were used to assess the home garden exposures. The studies were reviewed by HED and were found to meet most of the series 875 guidelines for post application exposure monitoring. The studies were performed using airblast sprayers while the proposed home garden applications would be made with LP handwand or hose end sprayers. Based upon experience with other fungicides, however, it is anticipated that DFRs resulting from handwand applications would be similar to DFRs from airblast applications. The initial DFR was assumed as 23% of the application rate and was based upon DFR Data for HS-1760 Site 3.

In addition, the following assumptions and exposure factors were used for assessing home garden post-application risks:

- The maximum application rates as listed in Attachment 1 for each crop were used for risk calculations as there are no use data available for home gardeners.
- The transfer coefficient (TC) is 10,000 cm^2/hr as stated in the Residential SOPs.
- The daily exposure duration for tasks performed in the home garden or home orchard are expected to be 40 minutes per day as stated in the Residential SOPs.

The MOEs are summarized in Table 9.2. The myclobutanil MOEs for all of the home gardener post-application scenarios are greater than the target MOE of 100 and are not of concern.

Table 9.2. Myclobutanil Post-Application Risks for Home Gardeners.

Crop	Application Rate (lb ai/A)	DAT 0 DFR (ug/cm^2)	TC (cm^2/hr)	Exposure Time (hours/day)	Dose (mg/kg/day)	Dermal MOE
Home Garden Ornamental Plants and Vegetables	0.25	0.65	10000	0.67	0.031	320
Home Orchard Fruit Trees	0.25	0.65	10000	0.67	0.031	320

9.3 "Pick Your Own" Post-application Exposures and Risks: "Pick your own" exposures can occur at commercially operated "pick your own" strawberry farms and orchards where myclobutanil has been applied. To address these risks, post-application exposure for pick your own strawberries and tree fruit were assessed based upon the Residential SOP 15.0 for "pick your own" strawberries. The DFR data that were used for the home gardener post-application risks were also used to assess "pick your own" exposures . The following assumptions and exposure factors were used for assessing "pick your own" post-application risks:

- The maximum label rates as listed in Attachment 1 for strawberries and tree fruit was used.
- The TC is 10,000 cm^2/hr as stated in the Residential SOPs.
- The daily exposure duration for "pick your own" strawberries is 4 hours as stated in the Residential SOPs.
- The daily exposure duration for "pick your own" tree fruits is 2 hours.

The myclobutanil MOEs are summarized in Table 9.3. The myclobutanil MOEs for the "pick your own" scenarios are greater than the target MOE of 100 and are not of concern. The risks for pick your own exposures are conservative because that scenario is based upon a screening-level TC and a dermal absorption factor of 50%. This risk could be refined by examining the recently submitted Agriculture Research Task Force (ARTF) TC studies and calculating TCs that match the clothing worn by pick your own customers.

Table 9.3. Myclobutanil Post-Application Risks for Pick Your Own Crops.

Crop	Application Rate (lb ai/A)	DAT 0 DFR (ug/cm^2)	TC (cm^2/hr)	Exposure Time (hours/day)	Dose (mg/kg/day)	Dermal MOE
Fruit Trees	0.25	0.65	10000	2	0.09	110
Strawberries	0.125	0.325	10000	4	0.093	110

9.4 Residential Turf Post-Application Exposure and Risks: The following exposure scenarios are assessed for residential post-application risks:

1 - Toddlers Playing on Treated Turf
2 - Adults Performing Yardwork on Treated Turf
3 - Adults Playing Golf on Treated Turf

A TTR study was used to assess the turf exposures. The field portion of this study was in North Carolina and California. This study was reviewed by HED and was found to meet most of the series 875 guidelines for post application exposure monitoring. The initial TTR for dermal exposures was assumed to be 2.4% of the application rate and was based upon an average of the DAT-0 and DAT-3 data for the California site. The following assumptions and exposure factors were used for assessing turf post-application exposure risks:

- The turf exposures were considered to be short- and intermediate-term in duration because myclobutanil can be used only 16 times per year and dissipates fairly rapidly with a half-life of 8.5 days. Acute exposures from granule ingestion were not assessed because there is no endpoint for acute dietary exposures for the general population, which includes children.
- The application rates of 0.62 and 1.36 lb ai/A were used for calculating short/intermediate term risks. The rate of 0.62 lb ai./A is from the Chemsico product labels (such as 9688-123 and 9688-165) and the rate of 1.31 lb ai/A is from non-Chemsico labels (such as 62719-463).
- The initial TTR for dermal exposures was assumed to be 2.4% of the application rate and was based upon an average of the DAT-0 and DAT-3 data for the California site. All of the data, including the two outliers, were included in this average, however if the outliers had not been included, the TTR would still have been the same (2.4%) because the outliers offset each other;
- 5% of the application rate has been used to calculate the 0-day residue levels used for defining risks from hand-to-mouth behaviors, measured TTR values are not used because of differences in transferability versus what would be expected during hand-to-mouth behaviors;
- 20% of the application rate has been used to calculate the 0-day residue levels used for defining risks from object-to-mouth behaviors, measured TTR values are not used because of differences in transferability versus what would be expected during object-to-mouth behaviors, a higher percent transfer has been used for object-to-mouth behaviors because it involves a teething action believed to be more analogous to DFR/leaf wash sample collection where 20%is also used;
- The Jazzercise approach is the basis for the dermal TCs as described in HED's Series 875 guidelines, SOPs For Residential Exposure Assessment, and the 1999 FIFRA SAP Overview document. This approach was used for toddlers on turf and adults on athletic fields;
- Soil residues are contained in the top centimeter and soil density is 0.67 mL/gram;
- Three year old toddlers are expected to weigh 15 kg;
- Hand-to-mouth exposures are based on a frequency of 20 events/hour and a surface area per event of 20 cm^2 representing the palmar surfaces of three fingers;

- Saliva extraction efficiency is 50% meaning that every time the hand goes in the mouth approximately ½ of the residues on the hand are removed;
- Risk values (*i.e.*, MOEs) for the different kinds of toddler exposures to turf (dermal, hand-to-mouth, object-to-mouth, and soil ingestion) were added together per HED policy as discussed in the ExpoSac Meeting Minutes. These exposures are typically added together when chemicals are used on turf because it is logical they can co-occur;
- Golfers have been assessed using a TC of 500 cm^2/hour;
- For golfer assessment it was assumed that the tees, greens and fairways are treated and that the exposure time per day would be four hours.

The myclobutanil MOEs for toddler and adult exposures are summarized in Table 9.4. The myclobutanil MOEs for toddler exposures at day 0, expressed as the total MOE, is 60 when the application rate is 1.36 lb ai/A and it is 140 when the application rate is 0.62 lb ai/A. The dermal pathway is the risk driver, which causes the total MOE to be below the target MOE of 100 at the higher application rate. The myclobutanil MOEs for adult dermal exposures are above 100 regardless of which application rate is used.

It should be noted that the high rate of 1.36 lb ai/A is from the Eagle® 20EW label (EPA Reg. No. 62719-463) that appears to be primarily intended for turf use on golf courses because it has the statement "A systemic, protective and curative fungicide for disease control in turf grass (including golf course fairways, roughs, tee boxes and greens)." The risk could be refined if a label statement could be added to the turf product labels to specify at maximum application rate of 0.62 lb ai/A on residential turf.

Table 9.4. Toddler and Adult MOEs for Post-Application Exposure to Turf Treated with Myclobutanil.

Exposure Scenario	Application Rate (lbs ai/A)	Dermal TTR (ug/cm^2)	Dermal Dose	Hand-to Mouth Dose	Object to Mouth Dose	Soil Ingestion Dose	Total Dose (mg/kg/day)	Total MOE*
Toddlers								
Playing on Lawns	1.36	0.37	0.127	0.020	0.0051	0.000068	0.152	65
	0.62	0.17	0.0579	0.0093	0.0023	0.000031	0.0695	140
Adults								
Heavy Yardwork	1.36	0.37	0.076	Not applicable				130
Playing Golf			0.0052					1900
Heavy Yardwork	0.62	0.17	0.035	Not applicable				290
Playing Golf			0.0024					4200

*The NOAEL is 10 mg/kg/day for dermal and incidental oral exposures.

10.0 Aggregate Risk

Aggregate risk assessments were performed for acute (food and drinking water), short-term (food, drinking water and residential), intermediate-term (food, drinking water and residential), and chronic aggregate exposure (food and drinking water). Long-term and cancer aggregate risk assessments were not performed because, based on the current and proposed use patterns, HED does not expect residential exposure durations that would result in long-term exposures and myclobutanil is not carcinogenic. All potential exposure pathways were assessed in the aggregate risk assessment.

10.1 Acute Aggregate Risk Assessment (Food and Drinking Water): The acute aggregate risk assessment takes into account exposure estimates from dietary consumption of myclobutanil (food and drinking water). Dermal, inhalation, and incidental oral exposures resulting from short-term residential applications are assessed separately. The acute dietary exposure estimates are below HED's level of concern (<100% aPAD) at the 95th exposure percentile for females 13-49 years old (4.2% of the aPAD). Therefore, the acute aggregate risk associated with the proposed uses of myclobutanil does not exceed HED's level of concern for females 13-49 years old.

10.2 Short-Term Aggregate Risk Assessment (Food, Drinking Water and Residential): The short-term aggregate risk assessments estimate risks likely to result from 1-30 days of exposure to myclobutanil residues in food, drinking water, and residential pesticide uses. In aggregating short-term risk, HED considered background chronic dietary exposure (food and drinking water; see Table 8.1) and short-term, non-dietary oral and/or dermal exposures (see Tables 9.1-9.4).

For adults, there is potential for short-term dermal and inhalation handler exposure, and short-term dermal post-application exposures from the residential uses of myclobutanil, including orchards, "pick your own" gardens, home fruit and vegetable gardens, and treated turf. However, the handler and post-application exposures were not combined as the likelihood of the residential homeowner experiencing both short-term handler and post-application exposure to myclobutanil is unlikely (it is current ExpoSAC policy not to combine handler and post-application exposures for these scenarios due to the conservative nature of each assessment alone). For children/toddlers, short-term dermal and non-dietary oral post-application exposures may result from dermal contact with treated turf as well as non-dietary ingestion/hand-to-mouth transfer of residues from turf grass.

For the general U.S. population and children/toddlers, the total food and residential short-term aggregate MOEs are listed in Table 10.1. For the general U.S. population, all short-term MOEs are greater than 100; and, therefore, do not exceed HED's level of concern (MOE <100).

For children/toddlers, the short-term aggregate MOE is 63 for the "playing on lawn" scenario using the turf application rate of 1.36 lb ai/A, but the MOE is 130 for the same scenario using the 0.62 lb ai/A application rate. It should be noted that the high rate of 1.36 lb ai/A is from the

Eagle® 20EW label (EPA Reg. No. 62719-463) that appears to be primarily intended for turf use on golf courses because it has the statement "A systemic, protective and curative fungicide for disease control in turf grass (including golf course fairways, roughs, tee boxes and greens)." The short-term aggregate risk could be refined if the myclobutanil turf labels are amended to specify at maximum application rate of 0.62 lb ai/A on residential turf.

10.3 Intermediate-Term Aggregate Risk Assessment (Food, Drinking Water and Residential): The intermediate-term aggregate risk assessment estimates risks likely to result from 1 to 6 months exposure to myclobutanil residues in food, drinking water, and residential pesticide scenarios. In aggregating intermediate-term risk, HED considered background chronic dietary exposure (food and drinking water) and intermediate-term, non-dietary oral and/or dermal exposures (see Tables 9.1-9.4).

For adults, intermediate-term post-application exposures may result from dermal contact with treated fruits and vegetables at "pick your own" gardens, treated home fruit and vegetable gardens and treated turf. As mentioned previously, since myclobutanil is applied at 7- to 14-day intervals, only short-term exposure is expected for the residential handler. Therefore, no aggregate intermediate-term exposure for the adult handler was performed. For toddlers, intermediate-term dermal and non-dietary oral post-application exposures may result from dermal contact with treated turf as well as non-dietary ingestion/hand-to-mouth transfer of residues from turf grass.

However, as the NOAEL (10 mg/kg/day) from a 2-generation reproduction toxicity study in rats was used for assessing short- and intermediate-term dermal, inhalation and incidental oral exposures, the short-and intermediate-term aggregate risk estimates from the post-application exposure scenarios are the same for the general U.S. population and children/toddlers (see Table 10.1).

Table 10.1. Short- and Intermediate-Term Aggregate Risk Calculations for Myclobutanil.

Population Subgroups	Exposure Scenario	NOAEL (mg/kg/day)	Level of Concern[1]	Max Exposure[2] (mg/kg/day)	Average Dietary Exposure (mg/kg/day)	Residential Exposure[3] (mg/kg/day)	Aggregate MOE (dietary and residential)[4]
Short-Term Handler Exposures							
General US Population	Hose End Sprayer - Mix your own	10	100	0.1	0.003842	0.054	170
Short- and Intermediate-Term Post-Application Exposures							
General US Population	Home Gardens	10	100	0.1	0.003842	0.031	290
	"Pick Your Own" Fruit Trees					0.09	110
	Turf - Heavy Yardwork (1.36 lb ai/A rate)					0.076	130
	Turf - Playing Golf (1.36 lb ai/A rate)					0.0052	1100
Children 1-2 years old	Turf - Playing on Lawn (1.36 lb ai/A rate)				0.007697	0.152	63
	Turf - Playing on Lawn (0.62 lb ai/A rate)					0.0695	130

[1] The level of concern (target MOE) includes 10X for interspecies extrapolation and 10X for intraspecies variation.
[2] Maximum Exposure (mg/kg/day) = NOAEL/Target MOE
[3] Residential Exposure = [Oral exposure + Dermal exposure + Inhalation Exposure].
[4] Aggregate MOE = [NOAEL ÷ (Avg Dietary Exposure + Residential Exposure)]

10.4 Chronic Aggregate Risk Assessment (Food and Drinking Water): The chronic aggregate risk assessment takes into account average exposure estimates from dietary consumption of myclobutanil (food and drinking water) and residential uses. However, due to the use patterns, no chronic residential exposures are expected. Therefore, the chronic aggregate risk assessment includes exposure from food and drinking water only. The chronic dietary exposure estimates are below HED's level of concern (<100% cPAD) for the general U.S. population (15% of the cPAD) and all population subgroups (see Table 8.1). The most highly exposed population subgroup is all infants (<1 year old) at 36% of the cPAD. Therefore, the chronic aggregate risk associated with the proposed uses of myclobutanil does not exceed HED's level of concern for the general U.S. population or any population subgroups.

11.0 Cumulative

The Agency did not perform a cumulative risk assessment as part of this tolerance action for myclobutanil. However, the Agency does have concern about potential toxicity to 1,2,4-triazole and two conjugates, triazole alanine and triazole acetic acid, metabolites common to most of the triazole fungicides. To support the extension of existing parent triazole-derivative fungicide tolerances, EPA conducted an interim human health assessment for aggregate exposure to 1,2,4-triazole (M. A. Doherty, "Interim Human Health Risk Assessment of 1,2,4-Triazole to Support Tolerance Extensions and New Section 18 Soybean Tolerances for Triazole-Derivative Fungicides," June 29, 2004, DP Barcode D304288). The exposure and risk estimates presented in this assessment are overestimates of actual likely exposures and therefore, should be considered to be highly conservative. Based on this assessment the EPA concluded that for all exposure durations and population subgroups, aggregate exposures to 1,2,4-triazole are not expected to exceed its level of concern. This assessment should be considered interim due to the ongoing series of studies being conducted by the U.S. Triazole Task Force (USTTF). Those studies are designed to provide the Agency with more complete toxicological and residue information for free triazole and are expected to be submitted to the Agency in the future. Upon completion of review of these data, EPA will prepare a more sophisticated assessment based on the revised toxicological and exposure databases.

12.0 Occupational Exposure

Occupational exposure and risk assessment - DP# 328188, M. Dow

Based upon the proposed use patterns (see Attachment 1), short-term (1-30 days) handler exposures and short- and intermediate-term post-application exposures are expected for the occupational worker.

12.1 Occupational Handler Exposure and Risk: Based upon the proposed use patterns, HED believes that the most highly-exposed occupational pesticide handler exposures are for a mixer/loader, loading wettable powder with water soluble packages and an applicator using open-cab, air-blast machinery. It is expected that some private applicators may perform all tasks, that is, mix, load and apply the material. However, HED ExpoSAC draft SOP (29 March 2000) directs that although the same individual may perform all tasks, in some cases they shall be assessed separately.

The available exposure data for combined mixer/loader/applicator scenarios are limited in comparison to the monitoring of these two activities separately. These exposure scenarios are outlined in the PHED Surrogate Exposure Guide (August 1998). HED has adopted a methodology to present the exposure and risk estimates separately for the job functions in some scenarios and to present them as combined in other cases. Most exposure scenarios for hand-held equipment (such as handwands, backpack sprayers, and push-type granular spreaders) are assessed as a combined job function. With these types of hand-held operations, all handling activities are assumed to be conducted by the same individual. The available monitoring data support this and HED presents them in this way. Conversely, for equipment types such as fixed-

wing aircraft, groundboom tractors, air-blast sprayers, or high-pressure handwand sprayers, the applicator exposures are assessed and presented separately from those of the mixers and loaders. By separating the two job functions, HED determines the most appropriate levels of personal protective equipment (PPE) for each aspect of the job without requiring an applicator to wear unnecessary PPE that might be required for a mixer/loader (e.g., chemical-resistant gloves may only be necessary during the pouring of a liquid formulation).

No chemical-specific data were available with which to assess potential exposure to occupational pesticide handlers. The estimates of exposure to pesticide handlers are based upon surrogate study data available in PHED (v. 1.1, 1998). For pesticide handlers, it is HED standard practice to present estimates of dermal exposure for "baseline;" that is, for workers wearing a single layer of work clothing consisting of a long-sleeved shirt, long pants, shoes plus socks and no protective gloves as well as for "baseline" and the use of protective gloves or other PPE as might be necessary. The proposed product label involved in this assessment directs applicators and other handlers to wear the following PPE: long-sleeved shirt, long pants, shoes plus socks, chemical-resistant gloves and protective eyewear.

Table 12.1. Estimated Handler Exposure and Risk from the Use of Myclobutanil on Hops.

Unit Exposure[1] (mg ai/lb handled)	Application Rate (lb ai/A)[2]	Units Treated[3] Per Day (Acres)	ADD[4] (mg ai/kg bw/day)	NOAEL[5] (mg ai/kg bw/day)	Combined MOE[6]
Mixer/Loader - Wettable Powders with Water Soluble Bags					
Dermal: No Glove 0.021 LC With Glove 0.0098 LC Inhal. 0.00024 LC	0.25	40	Dermal: No Glove 0.003 W Glove 0.0014 Inhal 0.00004	10	No Glove 3,300 W Glove 6,900
Applicator - Airblast - Open Cab					
Dermal: No Glove 0.36 HC With Glove 0.24 HC Inhal 0.0045HC	0.25	40	Dermal: No Glove 0.051 W Glove 0.034 Inhal 0.00075	10	No Glove 190 W Glove 290

[1] Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Dermal = Single Layer Work Clothing **No Gloves**; Single Layer Work Clothing **With Gloves**; Inhal. = Inhalation. Units = mg ai/pound of active ingredient handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.

[2] Applic. Rate. = Taken from the IR4 petition for myclobutanil on hops

[3] Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; SOP No. 9.1. Science Advisory Council for Exposure; Revised 5 July 2000;

[4] Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated ÷ Body Weight (70 kg used for short-term dermal; 60 kg used for short-term inhalation).

[5] NOAEL = No Observable Adverse Effect Level: short-term dermal and inhalation NOAEL = 10 mg ai/kg bw/day.

[6] MOE = Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. Short Term MOEs are combined since the dermal and inhalation NOAELS were identified from the same study.

All short-term MOEs are >100. Since HED's level of concern for myclobutanil is for MOEs below 100, all worker exposures are expected to be below the level of concern.

12.2 Occupational Post-Application Exposure : It is possible for agricultural workers to have post-application exposure to pesticide residues during the course of typical agricultural activities. HED in conjunction with the ARTF has identified a number of post-application agricultural activities that may occur and which may result in post-application exposures to pesticide residues. HED has also identified TCs relative to the various activities that express the amount of foliar contact over time, during each of the activities identified. TCs are expressed as cm^2/hr. For hops, the highest TC is 2,000 cm^2/hr which results from harvest activities or stripping or training the vines. As a "screening-level" assessment, HED herein uses the 2,000 cm^2/hr TC.

The TCs used in this assessment are from an interim TC SOP developed by HED's ExpoSAC using proprietary data from the ARTF database (SOP # 3.1). It is the intention of HED's ExpoSAC that this SOP will be periodically updated to incorporate additional information about agricultural practices in crops and new data on TCs. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.

Lacking compound-specific DFR data, HED assumes 20% of the application rate is available as DFR on day zero after application. This is adapted from the ExpoSAC SOP No. 003 (7 May 1998 - Revised 7 August 2000).

The following convention may be used to estimate post-application exposure:

Average Daily Dose (ADD) (mg ai/kg bw/day) = DFR $\mu g/cm^2$ * TC cm^2/hr * hr/day * 0.001 mg/μg * 1/60 kg bw

and where:

Surrogate DFR = application rate * 20% available as dislodgeable residue * (1-D)t * 4.54 x 10^8 μg/lb * 2.47 x 10^{-8} A/cm^2 .

0.25 lb ai/A * 0.20 * (1-0)0 * 4.54 x 10^8 μg/lb * 2.47 x10^{-8} A/cm^2 = 0.56 $\mu g/cm^2$, therefore,

0.56 $\mu g/cm^2$ * 2,000 cm^2/hr * 8 hr/day * 0.001 mg/μg * 0.5 (% dermal absorption) ÷ 70 kg bw = 0.128mg/kg bw/day.

MOE = NOAEL ÷ ADD then 10 mg/kg bw/day ÷ 0.064 mg/kg bw/day = 156.

A MOE of 100 is adequate to protect agricultural workers from post-application exposures. Since the estimated MOEs are >100, the proposed use does not exceed HED's level of concern.

12.3 REI: Myclobutanil is classified in Acute Toxicity Category IV for acute dermal, acute inhalation and primary skin irritation. It is classified as Toxicity Category I for primary eye irritation and it is a "Positive" dermal sensitizer. The Rally® label lists the REI as 24 hours, which is sufficient to protect workers from excessive exposure.

cc: J. Tyler (RAB1), T. Dole (RRB1), M. Dow (RAB1)
RDI: RA Team (5/31/06); PV Shah (7/12/06); F. Fort (7/12/06)
J. Tyler: 809B: CM#2: (703)305-5564: 7509C: RAB1

Attachment 1. Summaries of Proposed Use Patterns.

Summary of Proposed Directions for Use of Myclobutanil on Hops.

Crop	Maximum Application Rate (lb. ai/A)		Maximum Number of Applications	RTI[1] (days)	PHI[2] (days)	Comments/Restrictions
	Per Application	Per Season				
Hops	0.25	2	8	7-10	14	None.

[1.] RTI = retreatment interval
[2.] PHI = preharvest interval

Summary of Proposed Directions for Home Garden Uses of Myclobutanil.

Crops		Proposed Home Garden Use Pattern - Chemsico Fungicide M (1.55% ai; EPA Reg. No. 9688-123)					Registered Agricultural Use Pattern Rally® 40W and Nova® 40W (40% ai; EPA Reg. No. 707-221) Chemsico Fungicide M ((1.55% ai; EPA Reg. No. 9688-123)				
		Application Rate (lb ai/A)1 *[fl oz/gal]*		Maximum Number of Applications	RTI (days)	PHI (days)	Application Rate (lb ai/A)		Maximum Number of Applications	RTI (days)	PHI (days)
		Per Application	Per Season				Per Application	Per Season			
Asparagus	*CA*	*0.127 [1.25]*	0.508 *[5.0]*	4	14	30	0.125	0.5	4	14	30
	all other states	0.127 *[1.25]*	0.127 *[1.25]*	1	na2	180	0.125	0.75	6	14	180
Almonds		0.20 *[0.5]*	0.60 *[1.5]*	3	21	90	0.19	0.6		7-10	160
Apples and Mayhaws		0.27 *[0.66]*	2.7 *[6.6]*	10	7-10	14	0.25	2.0	8	10-14	14
Berries	Blackberry, Raspberry, Loganberry	0.067 *[0.66]*	0.268 *[2.68]*	4	10-14	0	0.0625	0.25	4	10-21	0
	Currant, Gooseberry	0.127 *[1.25]*	1.02 *[10.0]*	8	10-14	0	0.125	1.0	8	10-14	0
Cucurbits		0.127 *[1.25]*	0.635 *[1.25]*	5	7-10	0	0.0625	0.6	10	7-10	0
Grapes		0.127 *[1.25]*	0.635 *[6.25]*	5	14-21	14	0.075-0.125	0.6	ns2	14-21	14
Peppermint, Spearmint		0.127 *[1.25]*	0.381 *[3.75]*	3	14-21	30	0.125	0.2	3	14-21	30
Snap Beans		0.127 *[1.25]*	0.508 *[5.0]*	4	7-10	0	0.125	0.5	4	7-10	0
Stone Fruit	Apricot, Plum, Prune	0.20 *[0.5]*	1.4 *[3.5]*	7	7-21	0	0.0625-0.15	1.1	ns	7-14	0
	Cherry, Nectarine, Peach	0.20 *[0.5]*	1.4 *[3.5]*	7	7-21	0	0.0625-0.15	1.3	ns	7-14	0
Strawberry		0.127 *[1.25]*	0.762 *[7.5]*	6	14-21	0	0.125	0.75	6	14-21	0
Tomato		0.10 *[1.0]*	0.40 *[4.0]*	4	21	0	0.1	0.5	5	21	0

[1] Assuming spray volumes of 100 gallons per acre (GPA) for asparagus, berries, conifer trees, grapes, mint, ornamentals, snap beans, strawberries, and tomatoes; 400 GPA for almonds, pome fruit, and stone fruit (Memo, T. Dole, D319227).
[2] na = not applicable; ns = not specified.